UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December17, 2002

MEMORANDUM

SUBJECT: EFED response to the RRTF's errors-only comments on the Agency document "Comparative Risks of Nine Rodenticides to Birds and Nontarget Mammals"

TO: John Pates, Chemical Review Manager
Susan Lewis, Branch Chief

FROM: William Erickson, Biologist
Douglas Urban, Senior Biologist
Environmental Risk Branch III, Environmental Fate and Effects Division

THRU: Stephanie Irene, Acting Chief
Environmental Risk Branch III, Environmental Fate and Effects Division

The Environmental Fate and Effects Division (EFED) has reviewed the Rodenticide Registrants Task Force's (RRTF) "errors-only" response to the Agency document "Comparative Risks of Nine Rodenticides to Birds and Nontarget Mammals" dated October 3, 2001. Their comments of December 10, 2001 were prepared by J.F. Hobson, MorningStar Consulting, on behalf of the RRTF. As stated in the Agency's October 23, 2001 cover letter for the assessment, the registrants' 30-day response should address only mathematical, computational, typographic, or other similar errors. Matters of policy, interpretation, or applicability of data will be addressed after the public comment period in accordance with the Agency's reregistration process for pesticides.

In response to error comments by the RRTF and rodenticide registrants, EFED has made necessary computational and/or typographical corrections. However, EFED notes that many comments relate to policy, interpretation, or applicability of data, and those comments will be addressed along with public comments after the 60-day public-comment period.

Page RRTF comment

i Hazard, not risk. In the Executive Summary, the authors of the *Comparative Risks of Nine Rodenticides to Birds and Non-target Mammals* (PRA) state the risks from brodifacoum and bromadiolone are high for mammalian predators and scavengers that feed on poisoned target species based on laboratory secondary hazard studies and field data. The relationship of these hazard studies to the potential for exposure, and thus risk, to these mammals from commensal uses has not been characterized; therefore, this assessment cannot be called a "risk" assessment and it is inappropriate to say that the "risk" is "high"...Presentation of laboratory secondary toxicity studies. The presentation of secondary toxicity in the laboratory is misleading and reflects a poor understanding of the concepts of hazard versus risk. These are actually a type of dose-response studies and how many animals die is related to the dose selection and not necessarily to the risk of the compound. Exposure in these lab studies is often not the same as (or sometimes even close to) exposure under actual field conditions. Furthermore, the protocols and test conditions (*e.g.*, target and non-target species, number of animals, period of feeding) used for these studies often differed significantly, therefore it is not appropriate to compare their results as if they were the same as acute LD_{50} studies or other "standard" guideline studies.

EFED response: This has been addressed in the revised document. As the RRTF knows, rodenticide baits are formulated to be lethal to rodents and a few other small mammals, and they are not selective to the target species. Although many factors influence which nontarget animals might be exposed to baits, many nontarget organisms are attracted to and consume grain-based baits. Predators and scavengers also feed on rats and mice or other target species, and they are not likely to avoid feeding on those that have eaten rodenticide bait. Thus, rodenticide baits also pose potential secondary risks. EFED believes that the potential for risks to birds and nontarget mammals is well established for some of these rodenticides.

The risk assessment is based on the available data. Registrants have not submitted the data that would be needed to assess the probability of exposure. These data have been outlined in a section on *Uncertainty and Data Needs* in the revised assessment. The methodology used is similar to that used in the Agency's "Comparative Analysis of Acute Risk From Granular Pesticides" (EPA 1992) and "A Comparative Analysis of Ecological Risks from Pesticides and Their Use: Background, Methodology, Case Study" (EPA 1998)[1]; both were reviewed by a FIFRA Scientific Review Panel. Concerning the latter analysis, the Panel noted the many scientific uncertainties in the method, yet agreed that it was a useful screening tool that provides a rough estimate of relative risk. The

[1] See December 8-9, 1998 http://www.epa.gov/scipoly/sap/1998/index.htm

Page RRTF comment

Panel made a number of helpful suggestions to improve the utility of the method, most of which are included here.

Risk conclusions are presented in tabular and graphical form based on two analyses of the available data. The first is a comparative ranking of the potential risk based on a comparative-analysis model, and the second is a tabular comparative rating of potential risk based on a qualitative "weight-of-evidence" assessment. Quantitative estimates of risk are used in both; however, the "weight-of evidence" assessment includes qualitative assessments of secondary risk based on mortality and other adverse effects reported in laboratory and field studies, operational control programs, and incident reports, as well as toxicokinetic data and residue levels reported in primary consumers. This approach is in concert with EPA's risk-assessment guidelines[2], where professional judgement or other qualitative evaluation techniques may be used to rank risks using categories such as low, medium, and high when exposure and effects data are limited or are not easily expressed in quantitative terms.

i Dietary data are available for mammals for bromadiolone and should be referenced.

EFED response: Dietary data are not required for mammals, and none are present for bromadiolone in EFED's toxicity database or the EPA/OPP Health Effects Division's toxicity database. Statements such as "are available" can't be addressed unless a citation is provided, such as an EPA MRID number for the study.

ii Incident data. The discussion of rodenticide wildlife incidents misrepresents the data and does not take into consideration the RRTF review, which noted that approximately one-third of incidents were redundant within the Environmental Incident Inventory System (EIIS) and many others are incorrectly attributed to anticoagulants. Summary numbers overstate the number of incidents and in a "weight of the evidence" argument the number of incidents should not be overstated. The authors must adjust the numbers appropriately.

EFED response: The RRTF has not identified a single redundant incident in the risk assessment. Stating that there are redundancies in the EIIS is misleading, because the EIIS is a database, and not everything listed in the database is cited in the assessment. The RRTF should address the incident data presented in the assessment, not that in the database.

[2] See Guidelines for Ecological Risk Assessment (EPA/630/R-95/002F, 1998) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12460

Page RRTF comment

ii Kit fox mortalities. This parenthetical reference is misleading, speculative, and inappropriate in the Executive Summary. The 9 Kit foxes were reported as mortalities. Of these, 7 mortalities were attributed to vehicular impact, and 2 were attributed to unknown causes (not anticoagulants). While low-level (trace) residues were found in 8 of 9 Kit foxes, attributing these mortalities to brodifacoum is unfounded and speculative and these statements must be removed from the PRA.

EFED response: This statement has been removed from the Executive Summary. However, it is not misleading or speculative to state that brodifacoum residue was detected in the liver of nine kit fox carcasses; that is fact, not speculation.

ii, 19, 150 Presence of liver residues. To state that brodifacoum, or other anticoagulants, have been "implicated" or "involved" in rodenticide incidents does not "affirm causality" (Ecological Risk Assessment (ERA) Guidelines at 86). Liver residues are a biomarker of exposure. In the initial phase of elimination, liver residues are independent of the magnitude of exposure and a poor correlate with toxicity, although they are persistent. Persistent low-level residues of brodifacoum, and bromadiolone, have been observed by the State of California in numerous feral coyotes and other animals in perfect health. This fact alone supports an inconsistency in association and a "basis for rejecting causality" (ERA Guidelines at 86). The statement should say, "residues of brodifacoum, or other anticoagulants, have been detected in wildlife incidents." The role of low-level residues (the case for the majority of residues reported in the EIIS) in these incidents is questionable.

EFED response: The issue of potential adverse effects to nontarget organisms from sub-lethal exposure to rodenticides is discussed in the assessment, and EFED notes that the lack of reproduction studies that could help characterize this potential adverse effect adds to the uncertainty of the analysis. These studies will be required through a data call-in.

ii Gastro-Intestinal Tract (GIT) should be established as an abbreviation and used consistently throughout the document.

EFED response: That correction had already been made in the revised risk assessment.

ii, iii Define numbers in parenthesis (9) after brodifacoum and (3) after bromadiolone. They appear to have no relationship to anything.

EFED response: These numbers are not present in the revised risk assessment.

iv, 89, Table 47 Risk presumptions in tables. EPA does not describe how the risk

Page RRTF comment

presumptions (*i.e.*, low, moderate, high) in the two tables were determined. They appear to have been set using risk summary value data; however, no rating scales or other discrimination criteria have been described.

EFED response: That has been addressed in the revised assessment. See also EFED's first comment above.

1 PCO vs. PCA. Reference to a Pest Control Operator (PCO) is incorrect. Currently, 40 C.F.R. Part 171 refers to a Pest Control Applicator (PCA) commercial and private. *See* 40 C.F.R. § 171.2.

EFED response: That correction has been made.

1, 2 Presumption of equal exposure. This is a critical error in the PRA. This is inappropriate and there is no justification made for this assumption. Exposure is a key factor in any risk assessment. This presumption makes the entire analysis a "hazard assessment" and not a "risk assessment." It is inappropriate to compare Section 24(c) registrations for field-use only and Section 18 island restoration uses with products labeled for commensal uses only. Besides inappropriately assuming equal exposure, this assumption also does not account for the large differential in market share among the products registered for commensal uses, a fact clearly stated in Table 1, page 2....Interchangeability of rodenticides. EPA's justification for a presumption of equal exposure is that it will allow for an evaluation of how risks (but actually hazard) might increase or decrease as one rodenticide is used instead of another. This means that EPA is assuming that all rodenticides can be used interchangeably and substituted for one another. This may be true for rodenticide <u>active ingredients</u>, but is clearly not the case for rodenticide end-use products which may have different formulations, bait strengths, target species, use sites, application methods and rates, use restrictions, and so on. This means that EPA's entire hazard analysis applies only to rodenticide active ingredients and has no meaning for evaluating the potential risks of end-use products because product-specific and use-pattern specific factors have not been accounted for through exposure assessments. This limits the usefulness of EPA's analysis from a risk management perspective because it is not possible to propose risk mitigation measures for active ingredients per se and it is inappropriate to propose them for end-use products without first evaluating product-specific risks.

EFED response: See previous EFED comments on hazard versus risk above. A section titled *Use and Exposure Considerations* has been added to the assessment. In this section, EFED explains the basis for its exposure calculations and its assumptions. In addition, the Agency does not know the quantity of rodenticides sold and applied in the U. S., although we have repeatedly requested this information from rodenticide registrants. The RRTF, in a conference proceedings (Kaukeinen et al. 2000), cites over-

Page RRTF comment

the-counter container sales for four of the nine rodenticides, but provides no information on geographical or state usage, urban versus non-urban use, quantity of active ingredient and bait sold, or any information on use by Certified Applicators. Submission of this information will help EFED refine it's risk assessment.

2 For Field Uses, include control of rats and voles under Zinc Phosphide.

EFED response: That information was included in Table 2 in the revised risk assessment.

3 Correct reference. Table 2, reference to EPA 1998 a,b should be referenced as EPA 1998 a,b Reregistration Eligibility Decision (RED).

EFED response: That correction has been made.

4 Spelling. Fourth line, "sties" should be "sites."

EFED response: That correction has been made.

7 SAP review of the Decision Table Analysis. The Scientific Advisory Panel (SAP) reviewed this approach and strongly recommended that the term Risk Quotient (RQ) as used here should be called a "hazard" quotient (HQ). The RRTF agrees and believes that the terminology should be changed throughout the document consistent with the SAP's comments (SAP Report No. 99-01A, Jan. 22, 1999).

EFED response: The recommendations presented to the Agency following a SAP review are just that, recommendations. The Agency must consider the recommendations in light of extant Agency policies and guidance. In this case, EPA's Guidelines for Ecological Risk Assessment[3] uses the term Risk Quotient to describe a simple comparison of a measure of exposure divided by a measure of toxicity. In addition, the same guidelines notes that risk quotients provide an efficient, inexpensive means of identifying high- or low-risk situations that can allow risk management decisions to be made without the need for further information. Further, subsequent to the aforementioned SAP review, another panel of scientists and risk assessors - the Ecological Committee on FIFRA Risk Assessment Methods (ECOFRAM), stated that RQs do not quantify risk but are useful for comparisons among alternative compounds.[4] Thus, no change in the terminology is needed.

---

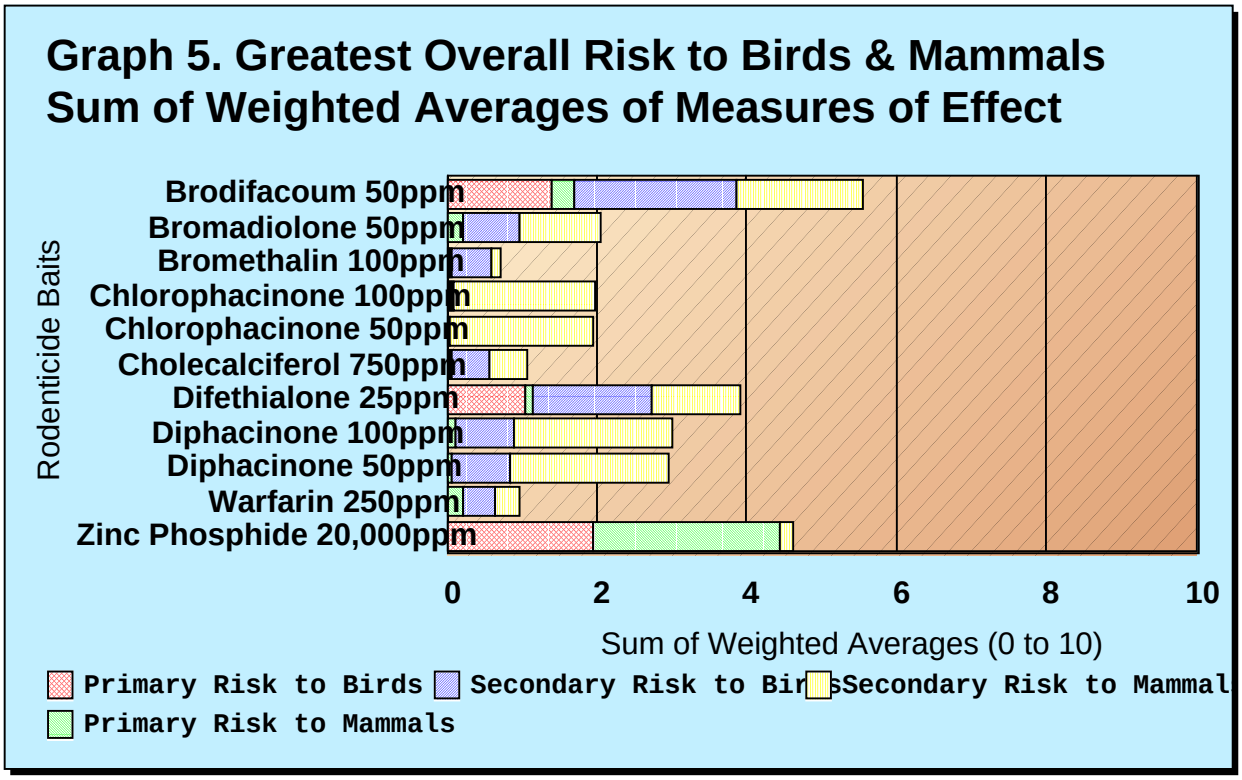
[3] Ibid.

[4] See ECOFRAM Terrestrial Draft Report, 1999 at http://www.epa.gov/oppefed1/ecorisk/

Page	RRTF comment
7	Definition of "effect." The term "measures of effect" as used in the Decision Table Analysis is in error because several of the "effects" discussed are not truly effects, but fate properties of the chemical. For example, it is inappropriate to use the terms "blood retention time" and "liver retention time" as measures of "effect" when the values being used in the assessment are actually elimination half-life values. The elimination and excretion of second-generation anticoagulants is biphasic and the initial phase is primarily from the liver. Research has shown that the residues involved in this terminal phase do not appear to contribute to coagulopathy. Further, at non-toxic concentrations the initial phase of elimination appears to be absent (Batten and Bratt, 1987). If this is true, then retention time in the liver, at low levels, is not an effect, but a marker of exposure. **EFED response:** While the retention time is not a direct measure of effect for secondary risk to birds and mammals, it is an important contributing factor. The combination of mean % mortality from secondary laboratory toxicity studies which characterizes the secondary toxicity from short-term exposures, and available data on retention time in both blood and liver which indicates how long toxic levels can persist in target animal tissues, can characterize the secondary risk to birds and mammals. If, however, retention time in blood and liver were removed from consideration in secondary risk for birds and mammals, the ranking of the rodenticides providing the greatest overall risk to birds and mammals would not change (As seen in the graphs below, brodifacouum, zinc phosphide and diafethialone provide the greatest overall risk in both cases. Figure 1 shows the comparison with retention time included in secondary risk. Figure 2 show s the comparison with retention times are removed from consideration. When retention times are removed from consideration, the sum of the weighted averages of measures of effect for brodifacoum increases, as does that for difethialone. In addition, the summary values for zinc phosphide and difethialone are almost equal - 4.63 and 4.60).

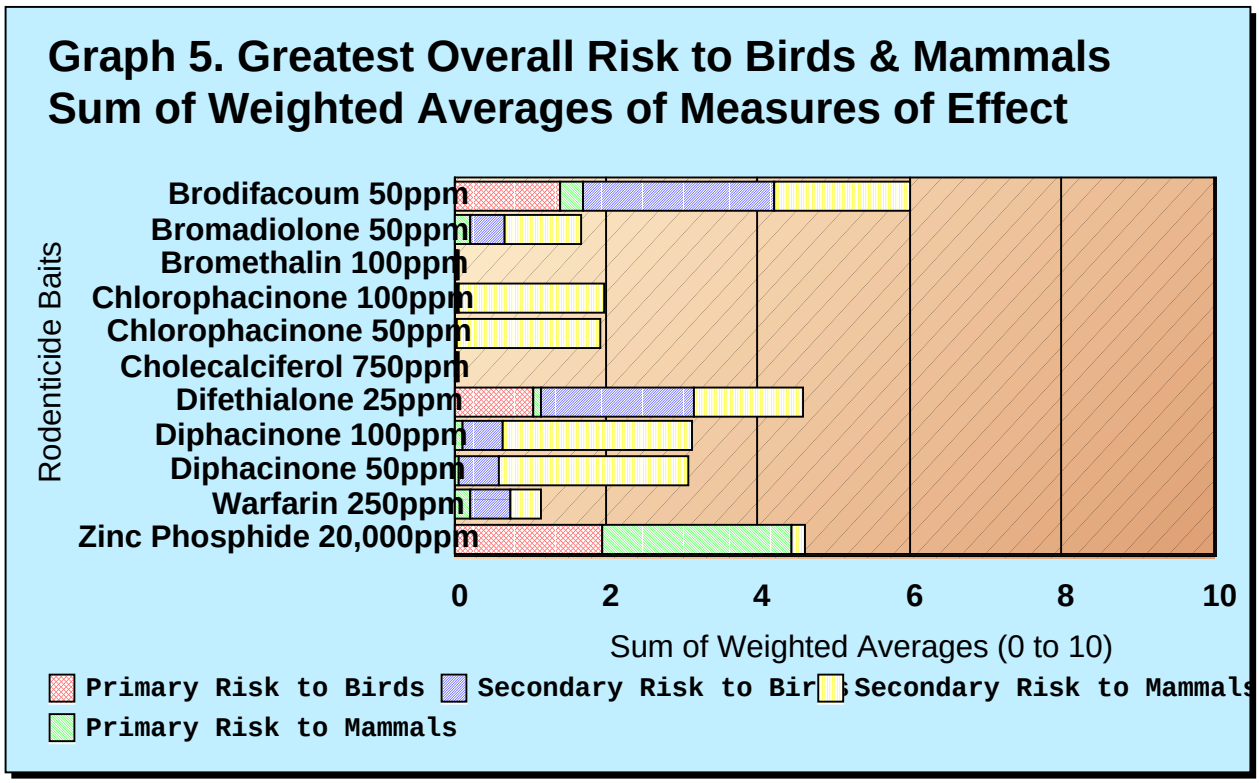
Page RRTF comment

Figure 1



Page RRTF comment

Figure 2



Page	RRTF comment

Page RRTF comment

7, Table 28 Measures of effect for primary risk to birds. The two measures of effect used in the analysis (dietary RQ and amount of bait needed to produce an LD_{50}) are not truly independent measures of effect. Both are based on the inherent toxicity of the active ingredient and, though different, are highly correlated. This amounts to "double counting" of the same measure of effect which skews the analysis.

EFED response: EFED disagrees that these measures of effect are correlated. The two measures of effect for primary risk to birds were tested for correlation using the 'Correlation and Regression Calculator' at http://www.ebook.stat.ucla.edu/cgi-bin/php.cgi/calculators/correlation.phtml, and the correlation coefficient was 0.272307, indicating little linear correlation.[5]

7, Table 40, Table 41 Use of two retention times as measures of effect. Blood retention time and liver retention time are not independent measures of elimination (half-lives). The values for the two retention times are usually not the same for any given species, but are highly correlated because of similarities in metabolism between different organs and tissues. Because the measures are correlated, it is inappropriate for both measures to be used in the analysis as this amounts to "double counting" the same endpoint**.** This "double counting" tends to exaggerate the magnitude of the summary values, either higher or lower, for all of the rodenticides, and makes those that are more persistent look worse than is actually the case**.** Furthermore, retention times make poor measures of effect. For example, they cannot distinguish differences in hazard between different bait strengths, as is apparent from the data presented in Tables 40 and 41.

EFED response: See previous EFED response on definition of effect on pages 7 & 8. In addition, the values are not "double counted"; each is given a weight one-half that of other measures (total weight of blood retention time = 5; total weight of liver retention time = 5; thus, total weight for retention time = 10), so that the two together have a weighting equal to other measures (i.e., 10). Further, EFED disagrees that retention times are correlated. The retention times for blood and liver were tested for correlation using the 'Correlation and Regression Calculator' at http://www.ebook.stat.ucla.edu/cgi-

[5] N.B. A correlation coefficient is a number between -1 and 1 which measures the degree to which two variables are linearly related. If there is perfect linear relationship with positive slope between the two variables, the correlation coefficient is equal to 1; if there is positive correlation, whenever one variable has a high (low) value, so does the other. If there is a perfect linear relationship with negative slope between the two variables, the correlation coefficient is equal to -1; this is a negative correlation, that is, whenever one variable has a high (low) value, the other has a low (high) value. A correlation coefficient of 0 means that there is no linear relationship between the variables.

Page RRTF comment

bin/php.cgi/calculators/correlation.phtml, and the correlation coefficient was 0.105801, indicating little linear correlation.[6]

7, Table 40, Table 41 Double counting of retention times in the analysis. In addition to the double counting issue discussed above, another problem with EPA's methodology is that it uses the same measures of effect for evaluating secondary risks to both birds and non-target mammals. Because the values for the blood and liver retention times are identical for both the bird and non-target mammal analyses, this leads to double weighting of these factors when the overall summary values are calculated. This double weighting exaggerates the previously described problem that these two measures of effect are not independent and further compounds their weighting in the analysis, giving them the equivalent of a quadruple weighting.

EFED response: See previous EFED response on definition of effect on pages 7 & 8. Again, the values are not "double counted"; each retention time (blood and liver) is given a weight of 2.5 when used to evaluate each secondary risk (birds and mammals). Thus, the total weight of blood retention time and the total weight of liver retention time is equal to a weighting equal to other measures (i.e., 10).

7 Secondary toxicity (hazard) vs. secondary risk. The mean % mortality from secondary toxicity studies are measures of hazard, not risk, because exposure in these lab studies is often not the same (or sometimes even close) to exposure under actual field conditions. Further, there is no consideration of the probability of exposure, a key aspect of any risk assessment.

EFED response: See previous EFED response on the potential for risk from rodenticides. We also note that to determine the probability of risk would require additional data on toxicity and exposure. Additional data needed to refine this risk assessment is presented in a section on *Uncertainty and Data Needs* in the comparative risk assessment.

7, Table 40, Table 41 Inappropriate use of data from secondary toxicity studies. The specific end-use products (including bait strengths), protocols, and test conditions (*e.g.*, target and non-target species, number of animals, period of feeding) used in these studies often differed significantly. Therefore, it is inappropriate to compare the results of mean mortality from one set of studies with those from another set of studies as if they were performed under identical conditions.

[6] Ibid.

Page RRTF comment

EFED response: A number of laboratory tests using avian and mammalian predators and scavengers to test for mortality due to secondary exposure were available and used in this assessment. Their design and methods varied considerably adding unknown variability to their results and to the analysis. Pending the development of standard methods and testing requirements for these tests they provide the best data available. EFED has identified additional data needed to refine this risk assessment in a section on *Uncertainty and Data Needs*.

8 Assignment of importance and weights for importance. All measures of effect, except for two, were assigned a "high" measure of importance for the analysis. The two that were assigned a "medium" importance (half lives in blood and liver) are correlated so "persistence" was also indirectly given a "high" weighting due to double counting. There is no explanation, or rationale, given by EPA for the selection of importance (high, medium, low) for the different measures of effect or the weights assigned to the importance values (*i.e.*, high = 10, medium = 5, low = 3.33).

EFED response: See previous EFED responses on weighting on page 9, Use of two retention times as measures of effect, and on page 10, Double counting of retention times in the analysis. As noted on page 6 of the document, all measures of effect, except two, are assigned a "high" (10 out of 10) measure of importance for the rodenticide analysis. The half-life in blood and liver are each given a weight of "low" (2.5 out of 10) for analyzing secondary risks to birds and mammals, so that the overall importance of the persistence data (2.5 x 4=10) equals but does not exceed that of the mortality data. The intention was to weigh all measures of effects and all risks equally in the analysis. This would eliminate the introduction of any value judgements on the part of the risk assessors.

13 GIT. *See* GIT comment above for page ii.

EFED response: Previously addressed.

13 Categorizing second-generation rodenticides. Categorizing rodenticide active ingredients as "bad actors" is to use non-standard, subjective, and qualitative terminology in a regulatory document. It is not a scientific or regulatory term and therefore difficult to interpret in the regulatory context. The Pesticide Action Network (PAN) is not an official government organization and should not be used as a reference in this document without proper qualification. The World Health Organization (WHO) may state that the second-generation active ingredients are "extremely hazardous" (not representing high risk), but all formulations containing these active ingredients are highly diluted (20,000x) in formulation and as formulated products are Category IV (label word, *Caution*) for all five acute hazard indicators. This should be a key factor in

Page RRTF comment

any risk assessment and must be included in the PRA. Thus, the concepts of hazard and risk are again blurred and poorly delineated by the authors of this document.

EFED response: That descriptor was removed from the revised risk assessment. The RRTF is correct in stating that rodenticide baits are highly diluted from the pure active ingredient. Nonetheless, registered products have been tested and proven efficacious in killing target species (rats, mice, and other small mammals); even larger mammals, including humans, have died after ingesting formulated bait. According to the New York State Department of Environmental Conservation, deer died after consuming bait, and HED's toxicity database lists an incident in Indonesia in which 20 people died after consuming brodifacoum-treated rice intended and labeled for use as a rodenticide.

16 Correct acute toxicity data. Listing for Laboratory Rat, 2.5 and 2.1 should not be, as EPA found this study deficient and therefore unacceptable with a new study being required (EPA letter dated Feb. 6, 1992). In the replacement study, accepted by EPA, the laboratory oral LD_{50} for rats was 7.0 mg/kg. This number should be listed and used in later references.

EFED response: The RRTF provides no supporting documentation that this study is "unacceptable". The study is categorized as "supplementary" in the HED's toxicity database, and data from supplementary studies are used in OPP risk assessments.

29 Target species. Table 15 data citation Riedel *et al*., 1991 is incorrect. Target species is listed as mouse in table; in Literature Citations target is listed as voles. It should be noted, however, that there are no registrations for brodifacoum in the U.S. with voles as a target species.

EFED response: The RRTF provides no supporting documentation that this citation is incorrect. The information cited in the risk assessment is correct according to Joermann (1998).

30 Correct reference. Table 15 data citation Riedel *et al*., 1991 is footnoted with reference to Joerman, 1998. This is incorrect.

EFED response: The information is cited in Joermann (1998). The RRTF does not state why this citation is supposedly incorrect.

30 Correct residue data. Footnote a must be corrected. Data on residue levels in target species have been submitted to EPA (MRIDs 43534601 and 43534602). The data indicate the results of field trials conducted with diphacinone baits against the California ground squirrel -- the principal target species for which diphacinone is used in field applications. Genesis Laboratories, on behalf of the California Department of Food and

Page RRTF comment

Agriculture (CDFA), conducted these trials. As part of these trials, dead ground squirrels were collected and analyzed for diphacinone residues. For the 0.005% treatment (10 samples), mean whole body residues found were 1.4 ppm with a deviation of 0.8 ppm. For the 0.01% treatment (10 samples), mean whole body residues found were 1.4 ppm with a deviation of 0.7 ppm.

EFED response: Previously, EFED had no record of these studies but has since obtained copies from the Agency's microfiche files. The residue data from these studies are now included the residue data in the revised risk assessment.

35 Lower number of secondary studies. Last paragraph, sentence 3: In the Bullard, Thompson, and Holguin diphacinone study, accepted and cited by EPA for the liver retention time (of concern) -- 90 days, 30 rats were fed these same livers for 14 days and there were "0" deaths with no increase in the rats' prothrombin times. That would change the number of secondary studies on diphacinone to 4 studies and change the calculations to 19 (30%) of 63 tested mammals dying. To be scientifically consistent, mention of the results of this portion of the study should be made by EPA.

EFED response: The Rodenticide Cluster Reregistration Eligibility Decision (RED) issued in July, 1998, required secondary toxicity studies with a mammalian predator and an avian predator to support reregistration of 0.005% ai and 0.01% ai diphacinone baits. Four years have passed without the registrant addressing this data gap. Because the rat is a target species for rodenticides, citing rat data will not fulfill this secondary-toxicity requirement.

35 Dietary, not secondary studies. In general, studies with captive or laboratory animals where the chemical is provided to carnivores/omnivores as spiked meat or dog food preparations are not secondary toxicity studies. These are dietary exposure studies and these references should be removed from this section.

EFED response: EFED considers these studies as indicative of secondary toxicity. Nontarget predators and scavengers can be exposed to and adversely affected by rodenticides via dietary exposure to dead or moribund target organisms.

Table 37 Diphacinone retention/elimination. Data in Diaz and Whitacre, 1976 (which were discussed on the previous page) indicate that elimination of diphacinone in the rat is rapid and similar to chlorophacinone. These data were not included in Table 37 or in EPA's analysis, which relied only on elimination data for blood and liver. Instead, EPA used blood data from cattle and liver data from humans that indicated much higher retention times and produced much higher measure of effect values in Table 40. It is inappropriate to directly compare elimination data generated with cattle and humans with those generated with rats or other species because of interspecies variations in

Page RRTF comment

metabolism and study dosing regimens. It is also inappropriate to use cattle and human elimination data as measures of effect when neither of these are either target or non-target species being considered in the assessment.

EFED response: Those data are discussed in the risk assessment. The data tabulated are half-lives and retention times (days). Those values are not obtainable from Diaz and Whitacre (1976); as stated in the risk assessment, nearly a third of the dose administered was not recovered in that study.

Tables 40 & 41 Source of data not shown. EPA does not cite the source of the retention time values listed in this table, which are subsequently used to derive measure of effect values. The values cannot be verified without this information.

EFED response: Attachment C states the source of data used in the decision analysis.

41 GIT. *See* GIT comment above for page ii.

EFED response: Previously addressed.

45, 46 2 gram pellets, erroneous. Describing the "average pellet" weight as 2 grams is in error by an order of magnitude or more and the large number of LD_{50}s per pellet is incorrect and misleading. For example, Talon 3/16 inch pellets weigh, on average, 0.2 g, and a smaller 3/32 inch pellet that weighs less is also available. With the exception of mouse-sized or smaller animals, it is not true that one or two pellets of brodifacoum bait will kill a single animal. Ingestion of 7 to 14 of the larger pellets is required to kill a rat and considerably more for the larger non-targets. This error is repeated throughout the document and leaves a false impression that one granule will kill an organism. All assumptions, calculations, and conclusions based on this statement must be corrected.

EFED response: This correction has been made in the revised risk assessment.

46, Table 26 Source of data not shown. EPA does not cite the source of the LD_{50} values listed in this table, which are subsequently used to derive measure of effect values. The values cannot be verified without this information.

EFED response: Attachment C states the source of data used in the decision analysis.

47 b/c The dietary RQs should be defined as HQs. The footnotes do not provide sufficient background and justification for the rate (100% or 20% intake of daily intake) or timeframe of exposure (*i.e.*, "several days"). The bottom line is that the concentration in the bait does not provide an estimate of exposure and the PRA does not provide a case

Page RRTF comment

for the probability of actual exposure. The latter is dependent on use pattern that is ignored in these calculations.

EFED response: See previous EFED responses on page 2, for Hazard not risk, and page 5 for Presumption of equal exposure.

47, Table 27 Source of data not shown. EPA does not cite the source of the LC_{50} values listed in this table, which are subsequently used to derive measure of effect values. The values cannot be verified without this information.

EFED response: Attachment C states the source of data used in the decision analysis.

48, Table 28, Figure 1, Attachment C Error in calculation of summary values. EPA has made a significant calculation error when calculating the summary values for primary risks to birds due to a mistake in weighted average values for the second measure of effect (grams of bait needed for a 50 g bird LD_{50} dose). EPA calculated the weighted average values for this measure of effect by indexing to the least toxic rodenticide (diphacinone 50 ppm) rather than the most toxic one as was done for the other measures of effect [Note: similar incorrect calculations were also done for primary risk to mammals, this will be discussed below]. EPA's method of calculation is presented on page 133 (Step 3, substep B) in Attachment C. This method skewed results so that both brodifacoum and zinc phosphide were given the same weighted average of 5.0, even though it is clear from the data for this measure of effect that zinc phosphide (LD_{50} dose = 0.03 g) is almost 10 times more hazardous than brodifacoum (LD_{50} dose = 0.26 g) and should be weighted accordingly. Results for the other rodenticides were also skewed in a similar manner. The table below presents EPA's values and corrected results based on indexing to the most toxic rodenticide by using the inverse of the LD_{50} dose (*i.e.*, weighted averages are calculated by indexing to the value of 33.33 g for zinc phosphide, rather than 400 g for diphacinone 50 ppm). After the values have been corrected, zinc phosphide has the highest ranking based on summary values.

EFED response: The Agency agrees with using the inverse of the number of bait pellets equal to an LD_{50} dose and indexing based on the highest number. The necessary corrections have been made in the revised risk assessment.

49 Incorrect presentation of bait concentrations. In all graphs and figures in the document, the assay of active ingredient is listed incorrectly for all products as x mg. This should be correctly listed as x mg/kg bait or ppm. This must be corrected as it gives the reader a false sense of what is being stated. These are concentrations (*i.e.*, rates of exposure), not fixed amounts.

EFED response: A change to ppm has been made.

Page RRTF comment

51 Table 29. The footnote for Coumatetralyl and Difenacoum should be (b) not registered in the United States

EFED response: Correction has been made.

54 Nomenclature. The taxonomy entry for Chaffinch should have the scientific name *Fringilla coelebs* following the entry as this is the first reference to the species.

EFED response: Correction has been made.

55 Speculation of sub-lethal effects. The authors of the PRA refer in several places to speculations by authors that there might be long-term physiological or behavioral effects. There are no substantive data that support these sub-lethal effects. All of the references cited by EPA regarding this issue are speculative and no data are available. The only behavioral effects are associated with lethal levels of anticoagulants. Discussion of sub-lethal effects must be highly qualified as speculative in this document.

EFED response: We disagree that all the references cited indicating the potential for sublethal effects are speculative. EFED acknowledges that additional data are needed to confirm the reasoned arguments that sublethal effects adversely impact nontarget organisms exposed to rodenticides. Toward this end, and as previously stated, the potential for adverse sublethal effects will be addressed through a data call-in.

56 Products not comparable. Paragraph 2. "calciferol" (vitamin D2) in the UK, is an entirely different product and is unrelated to the cholecalciferol (vitamin D3) in the U.S. This comparison should be removed as irrelevant.

EFED response: The products may be different, but the toxicologically active metabolites may have similar effects, including hypercalcemia and degeneration of bone matrix. Eason et al. (2000) state that cholecalciferol (Vitamin D3) must undergo metabolic conversion to 25-hydroxycholecalciferol (25OHD) to gain biological and toxicological activity. If the RRTF has information that calciferol metabolizes in a different manner or does not have comparable toxicological effects in animals, documentation should be provided.

56 Using correct toxicity data. Second paragraph from the bottom, reference to the decision table analysis should be based on the above-mentioned 7.0 mg a.i./kg acute oral dose.

EFED response: As previously discussed, EFED has checked the values, and the values used in the risk assessment are correct.

Page RRTF comment

57 Using correct toxicity data. Table 31. Diphacinone should be listed as 7.0 mg a.i./kg. (acute oral rat), instead of the 2.3 found in the EPA unacceptable study. The entries in the table for diphacinone should be:

This, of course, changes the summary values for diphacinone. Diphacinone 100 ppm moves to under Chlorophacinone 100 ppm, and Diphacinone 50 ppm moves under Chlorophacinone 50 ppm.

EFED response: See previous comment.

57, Table 31 Source of data not shown. EPA does not cite the source of the LD_{50} values listed in this table, which are subsequently used to derive measure of effect values. The values cannot be verified without this information.

EFED response: LD50 values used in the comparative risk assessment are listed in the revised Table 31 in the revised risk assessment.

58-59, Table 32, Figure 2, Attachment C Error in calculation of summary values. EPA has made a significant calculation error when calculating the summary values for primary risks to mammals due to a mistake in weighted average values for the measure of effect (grams of bait needed for a 25 g mammal LD_{50} dose). EPA calculated the weighted average values for this measure of effect by indexing to the least toxic rodenticide (chlorophacinone 50 ppm) rather than the most toxic one as was done for the other measures of effect. This method skewed results so that both brodifacoum and zinc phosphide were given almost the same weighted average, even though it is clear from the data for this measure of effect that zinc phosphide (LD_{50} dose = 0.03 g) is almost 7 times more hazardous than brodifacoum (LD_{50} dose = 0.20 g) and should be weighted accordingly. Results for the other rodenticides were also skewed in a similar manner. The table below presents EPA's values and corrected results based on indexing to the most toxic rodenticide by using the inverse of the LD_{50} dose (*i.e.*, weighted averages are calculated by indexing to the value of 33.33 g for zinc phosphide, rather than 3.10 g for chlorophacinone 50 ppm). Note that because there is only one measure of effect for evaluating risk to non-target mammals, the summary values are identical to the average weighted values for this measure of effect.

EFED response: The Agency agrees with using the inverse of the number of bait pellets equal to an LD_{50} dose and indexing based on the highest number. The necessary corrections have been made.

59 Figure 2. Same changes as Figure 1.

EFED response: The necessary changes have been made.

Page RRTF comment

59 Spelling. Fifth line from the bottom, correct spelling is cholecalciferol.

EFED response: Correction has been made.

60 Correction of footnotes. Table 33 -- the footnotes for (c) and (d) are missing from the table.

EFED response: The footnotes have been added within the table.

61 Selective and misleading presentation of data. The entire presentation of the toxicokinetics (absorption, metabolism, and excretion) is based on a selective and misleading interpretation of the data. The half-life of residues of second-generation anticoagulants cannot be characterized by a single number. The elimination from the body is biphasic. The rapid initial (a-) phase (a few days) is related to toxicity and the extent of exposure in this phase is the determinant factor in toxicity. The PRA discusses the residues in various tissues and the longer b-phase of elimination (hundreds of days) leading the reader to conclude that toxic residues are present for hundreds of days. There are two distinct half-lives and it is incorrect and misleading to discuss toxic residues as having the longer half-lives (hundreds of days). The authors of the PRA, however, ignore discussion from the same articles referenced for residue data (*e.g.*, Batten and Bratt, 1987) that present observations that the b-phase is not dose-related and not related to toxicity (*i.e.*, coagulopathy). When exposure occurs at non-toxic levels, only the b-phase of elimination is evident, indicating that low-level exposure may occur without being toxicologically significant. This is an important point in a balanced and complete discussion of the toxicokinetics data.

EFED response: The existence of biphasic kinetics in the liver is now discussed in a comprehensive and balanced way in the document. However, the RRTF should be aware that not all studies have demonstrated biphasic elimination.

64 Correction. The first sentence on this page is incorrect. Two animals did not die in the top dose level. All animals that exhibited marked toxicity were euthanized according to the protocol. The authors of the PRA ignore one of the major points of this paper, that toxicity is associated with the rapid a-phase of clearance and not the b-phase of clearance. The b-phase residues are associated with long-term liver residues and are independent of dose. This makes liver residues, especially low-level residues, a good marker of exposure, but a poor indicator of causative agent.

EFED response: See previous comment. As previously noted, the issue of low-level exposure will be addressed through a data call-in.

Page RRTF comment

70 GIT. *See* GIT comment above for page ii.

EFED response: Previously addressed.

70 Secondary hazard vs. risk. The authors discuss laboratory data as a basis for determining secondary risk. This is not possible. Risk cannot be determined without an estimate or probability of exposure. As discussed by the SAP (SAP Report No. 99-01A, Jan. 22, 1999) in reviewing the Decision Analysis, this is a hazard assessment, not a risk assessment. The SAP Report states: *"The Panel encourages the Agency to change the term risk to "hazard." The calculation of the RQ does not include elements of risk. . . ."*

EFED response: See previous EFED responses above.

71, Table 40 Correction, Table 40. For diphacinone, secondary mortality, EPA has used an active ingredient blended rate of mortality of 9.0%. This should be a product-specific value, however. As in the previous Table 13, "Secondary Toxicity of Diphacinone to Birds . . .," it is clearly shown that there is a difference in secondary toxicity to the predator if the prey receives bait containing 50 ppm versus products or prepared diets with higher concentrations. When predators consume prey that fed upon bait containing 50 ppm or less, there is "0%" mean mortality to the secondary species. This demonstrates the problem of confusing active ingredient vs. formulated product and should be corrected before the PRA is released for public comment.

EFED response: Nine percent mean mortality was assigned to both formulations of diphacinone as a measure of secondary risk based on the assumption that the target would contain approximately the same residue regardless of which formulation it was exposed to. Data providing more detailed information by formulation is needed to refine this assessment.

72 Field data taken out of context. In this document, numerous types of field studies are referenced, but none of these studies are directly applicable to assessing the risks of products used to control commensal rodents (*i.e.*, "in and around buildings"). It is unclear to the reader that these field data are from research and development studies for products never registered or for localized island restoration projects. This false impression must be corrected prior to public release of this document.

EFED response: The Agency believes that the description of the field studies and their results provide accurate information on the effects of rodenticides outdoors and and does not leave the reader with a false impression. There is no clear distinction between commensal uses and field or other outdoor uses. Labels for commensal-use products do not limit bait placements to any specified distance from buildings, and "in and around buildings" may be interpreted differently among rodenticide users. Thus, some

Page RRTF comment

commensal uses, especially in rural areas, might have comparable exposure scenarios to some field uses.

73 Relevance of field studies conducted outside the United States. Studies such as Duckett, 1984, involving Asian owls in Malaysian oil-palm plantations, are not relevant to the labeled use in the United States. Asian owls are larger and take larger prey (*e.g.*, rats) than do North American owls. Rats were present due to the monoculture of this crop and owls were encouraged to inhabit the plantations using nest boxes. At the same time, anticoagulants are used to control rats. This is completely opposite of the use pattern labeled in the United States. Although some hazard information can be gleaned from such studies, there is no relevance to the exposure to wildlife from current use patterns (*i.e.*, commensal uses). This must be clearly stated.

EFED response: These studies are presented in a hazard context and confirm the potential for adverse effects of exposure. See also previous comment.

75 The author's use of unrelated data to justify a position that is incorrect and misleading. The "Incident Data Birds and Non-target Mammals," page 77 through 86 of the PRA is used as a reference. The author references the RRTF's proposal for a 0.7 ppm threshold of toxicity for brodifacoum in liver tissue -- a concept clearly based on brodifacoum data. The author cites a study, Savarie *et al*., 1979, in which liver tissue from coyotes was examined and found to contain residues of <0.7 ppm diphacinone. The use of unrelated data (brodifacoum vs. diphacinone) to justify a position (rejection of the toxicity threshold of 0.7 ppm based on brodifacoum data, the largest body of data for any of the rodenticides) is not scientifically justified.

EFED response: The reference to the diphacinone study was deleted from this discussion in the revised risk assessment. The RRTF is correct in stating that such a "threshold of toxicity" would need to be established for each of the nine rodenticides if the concept were to be of any value. Addressing the issue of adverse effects from sub-lethal toxicity also needs to be considered in such a threshold.

75 Inappropriate comparisons. Table 41. Decision Table Analysis for Secondary Risk to Bird. It is not scientifically justified to compare rodenticides, when values for Blood Retention and Liver Retention are taken from different species, *e.g.*, cattle and humans vs. rats.

EFED response: EFED acknowledges the variable nature of the retention data; however, these are the only data available. Additional data on retention in tissues of target organisms would greatly facilitate a refinement of the risk assessment.

76 Figure 4. The same correction as in previous figures.

Page RRTF comment

EFED response: The necessary changes have been made.

77 Errors in the EIIS database carry over to the PRA. The EPA, in conducting the PRA of anticoagulant rodenticides, emphasizes the number of wildlife mortality incidents reported to EPA, particularly by California and New York. EPA data on wildlife mortality incidents were obtained through a request for information by the RRTF under the Freedom of Information Act (FOIA). These data have been reviewed and analyzed by cross-referencing to EPA and state (California, New York, and other states) incident numbers, the report date, the species reportedly involved, the compound(s) reported, the number of individual mortalities reported per incident, tissue residue levels, the presence of raw data, the presence of necropsy information, the relative condition of carcasses, and any indication of intentional or unintentional misuse (off-label use) of the rodenticide products. The underlying data was also analyzed using a threshold of toxicity based on liver residues (Kaukeinen, Spragins, and Hobson, 2000) that differentiates residues that are clearly acutely toxic and very low residues that are simply a marker of exposure.

This analysis demonstrates that the toxicological and ecological significance of the wildlife mortality incident data for anticoagulant rodenticides is greatly overstated. There are numerous factors that restrict the number of wildlife mortality incidents that can be accurately attributed to anticoagulant rodenticides. There are as many as 30% redundant reports (*i.e.*, multiple reports of the same incident) in the EIIS database relative to anticoagulants. EPA conclusions relative to many incident reports are not supported by the underlying data. For many of the incident reports the residue levels of anticoagulants are very low and are not indicative of anticoagulant toxicity. Reported pathological observations are often not diagnostic of anticoagulant toxicity and often do not provide a basis for attributing mortality to anticoagulant rodenticides. The role of misuse (intentional or unintentional) is not consistently documented in incident reports, but may play a role in the many incidents attributable to anticoagulant rodenticides. The primary conclusion of this analysis is that the magnitude of reported incidents alleged to be caused by anticoagulant rodenticides is significantly over-estimated.

When incident numbers for the 226 incidents referred to in the PRA were requested by the RRTF, the authors did not have the incident numbers, suggesting that the analysis by the RRTF was not reviewed or considered by EPA prior to finalizing the current draft of the PRA. If the RRTF analysis of the EIIS database had been thoroughly reviewed, the incident numbers would have been obtained for comparison. The RRTF believes that the errors pointed out in the EIIS database constitute a serious error in the PRA and must be corrected before this document is released for public review.

EFED response: The RRTF's assertion that the authors did not provide incident tracking numbers is incorrect. Incident tracking numbers for all incidents cited in the assessment

Page RRTF comment

were provided (via the Special Review and Reregistration Division) to the RRTF when requested in November of 2001. The Agency is now aware of 258 rodenticide incidents.

81 Correct spelling is Contra Costa County.

EFED response: The change from "Contra costa County" to "Contra Costa County" has been made.

81 Unbalanced review of data. The authors of the PRA spend more than half of a page justifying the reference to one Golden eagle mortality arguing that it is a brodifacoum mortality with 0.04 ppm in the liver. Brodifacoum was only "implicated," however. This raises three important issues: 1) the majority of residues reported in wildlife are below 0.7 ppm in the liver and one-third are below 0.1 ppm, making interpretation of low-level residues a very important issue requiring a comprehensive, scientifically defensible discussion; 2) residues below 0.7 ppm are frequently reported in healthy feral animals; and 3) pathology is not diagnostic of anticoagulant toxicosis and cannot be used in combination with low-level liver residues as the determinative criteria of a causative agent in a wildlife mortality incident.

The majority of reported liver residues of anticoagulant rodenticides in the EIIS database are well below 0.7 ppm; therefore, it is important to understand the significance of such residues. If there is no consistency in association, causality cannot be confirmed and must be rejected. California and New York incident data were analyzed by the RRTF utilizing a threshold of 0.7 ppm brodifacoum (and possibly other anticoagulants) in liver. Applying this threshold to the data from both states (which is primarily for brodifacoum) indicates that approximately two-thirds of all incidents with residue data are below 0.7 ppm in the liver. One-third of incidents had reported liver residues below 0.1 ppm. The predominance of low-level residues in mortality reports emphasizes the importance of accurate interpretation of their significance. This merits a balanced discussion.

There are numerous reports in the literature and by state agencies that document measurable liver residues of brodifacoum and other anticoagulants in perfectly healthy feral animals. In the analysis of ten coyotes, the conclusion of an unpublished California Department of Fish and Game (CDFG) report was: "the residue concentrations in these otherwise healthy animals may suggest that background levels of anticoagulant rodenticides are found in urban carnivores…" (Table 81a) (p-2051, Hosea, 1999). In other incident reports by CDFG, however, lower level residues of second-generation anticoagulants are cited as diagnostic of the anticoagulant as the causative agent of observed mortality (Hosea, 1999). These inconsistencies demonstrate the difficulty of ascribing causality in these cases, and the value of agreed protocols for pathology and chemical analysis (Brown *et al*., 1996). Detection of low-level residues may represent

Page RRTF comment

the slow terminal phase of clearance with residues sequestered in the liver, and must be carefully interpreted with respect to any forensic, diagnostic, or toxicological significance. Long-term anticoagulant feeding studies in rats, such as with diphacinone, for example, failed to find consistent effects on clotting times or general health and feeding behavior at levels of 0.03 to 0.5 ppm over 90 days of continuous feeding (Elias and Johns, 1981).

All of the animals were free of any apparent trauma or disease, and necropsy revealed no evidence of hemorrhage (other than one hematoma caused by the administration of the lethal injection). All 5 of these animals carried residues of brodifacoum in the liver and 4 of the 5 carried multiple anticoagulant residues (Table 81b). It is apparent that liver levels of brodifacoum characterized in many wildlife reports as diagnostic of toxicity and fatality are also found as background levels in the livers of healthy wildlife.

Finally, low-level residues of anticoagulants are often used, regardless of the magnitude of the residue, to confirm pathological observations. In combination, these low-level residues and pathology cannot be used to determine that an anticoagulant rodenticide is the causative agent. Pathology is often the primary criteria in wildlife incident reports used to conclude anticoagulant toxicity. Although the lesions observed in incident reports may be indicative with anticoagulant toxicity, they are general and not diagnostic. Pathology, necropsy, and clinical signs of toxicity following anticoagulant exposure reported in published literature were compared by the RRTF to the information in the EIIS wildlife incident reports (Berny *et al.,* 1997; DuVall *et al.,* 1989; Elias and Johns *et al.,* 1981; Gray *et al.,* 1994; Hegdal and Colvin, 1988; Huckel *et al.,* 1988; Meehan, 1984; Newton *et al.,* 1990; Rammell *et al.,* 1984). The descriptions of anticoagulant toxicity in controlled studies were for the most part general. These descriptions include external hemorrhage and internal hemorrhage in a number of organs, including brain, kidney, lungs, heart, and gut. Major organs, including the liver, may exhibit diffuse pallor. First signs often include bloody diarrhea or urine. A number of articles cautioned that care must be taken in diagnosing anticoagulant poisoning both because obvious symptoms may be lacking and not every hemorrhagic lesion denotes anticoagulant poisoning. Other causes of coagulopathy noted in these articles include: infectious canine hepatitis, hemorrhagic disease of pigs, cows, and chicks, heat stroke, aflatoxicosis, vitamin K deficient diet, trauma, inherited clotting factor deficiencies, and consumption of naturally occurring anticoagulants (*e.g.,* dicumarol in sweet vernal hay).

In summary, pathologic observations should be used as secondary indicators of anticoagulant toxicity and not in combination with low-level anticoagulant residues. Although they may be indicative, they are not diagnostic. There are other causes of these generic types of lesions.

Page RRTF comment

EFED response: As previously stated, the issue of low-levels of residue will be addressed through a data call-in.

82 Correction. The reference Savarie *et al*., 1979 included oral doses of 0.63, 1.25, 2.5, 5, and 19 mg a.i./kg. Table 44 lists the doses as 0.63, 1.25, 2.5, 5, and 10 mg a.i./kg

EFED response: The doses listed in the table are correct. The doses are not cited in the text in the revised risk assessment.

83 Footnote for Dicoumarol is missing. This product is not registered in the United States as a rodenticide

EFED response: Footnotes are used only in the tables, not in the text. Dicoumarol is an anticoagulant compound.

87, Table 46 Errors in EPA's calculations (Table 46). EPA has made a significant calculation error when deriving the summary values for primary risks to both birds and non-target mammals. EPA incorrectly calculated the weighted average values for the following measures of effects: 1) grams of bait needed for a bird LD_{50}; and 2) grams of bait needed for a non-target mammal LD_{50}. Values were indexed to the least toxic rodenticides rather than the most toxic ones. This error changes the overall rankings of the nine rodenticides, as well as the magnitude and spread of the summary values among the nine products. The correct summary values are presented in Table 5 (Note: this is a revised Table 46 from the PRA). Based on the new overall summary values, brodifacoum is still ranked first (*i.e.*, "most hazardous"). Zinc phosphide, formerly fifth, is now ranked second, although its summary value is almost the same as brodifacoum. The two diphacinone baits are now ranked fourth and fifth overall as opposed to formerly being ranked as third and sixth, and their overall summary values are lower. The two chlorophacinone baits are now ranked eighth and ninth overall versus previous rankings of ninth and eleventh, but again the relative numbers and differences are lower than before, indicating less overall hazard than previously expressed.

EFED response: The necessary changes have been made.

88 Figure 5. The same correction as previous figures.

EFED response: The necessary changes have been made.

89 Figure 6. The same correction as previous figures.

EFED response: The necessary changes have been made.

Page RRTF comment

90, Figure 7 Flaw in sensitivity analysis. Because several of the measures of effect were significantly correlated, the sensitivity analysis would not be expected to show differences in rankings when values for the measures of effect were varied.

EFED response: EFED disagrees that several the measures of effect are in fact correlated. Specifically, the two measures of effect for primary risk to birds and the retention times for blood and liver were tested for correlation using the 'Correlation and Regression Calculator' at http://www.ebook.stat.ucla.edu/cgi-bin/php.cgi/calculators/correlation.phtml, and the correlation coefficients were 0.105801 and 0.272307, respectively, indicating little linear correlation.[7]

91 Distinctions between 50 and 100 ppm baits. EPA states that distinctions cannot be made between 50 ppm and 100 ppm chlorophacinone and diphacinone baits using the incident data, "but the 100 ppm baits are likely to present greater risk than 50 ppm baits." This may seem like an obvious statement, but in fact it may not be true because of differences in the formulations and use patterns between the baits containing 100 ppm and 50 ppm of these active ingredients. It is not correct to assume that they are used interchangeably. Some pelleted baits containing 50 ppm active ingredient are used "in and around" homes for commensal control while other 50 ppm grain-based baits are used in bait stations for control of ground squirrels and other field rodents. The 100 ppm baits are grain-based and only used in agricultural settings for control of ground squirrels and field rodents. The 100 ppm baits are applied by broadcast methods (mechanical or hand) and are not used in bait stations. Secondary risks to birds and non-target mammals are dependent, in part, on residues in the target species and could potentially be higher for 50 ppm baits because of greater bait availability in bait stations and many other factors.

EFED response: EFED believes that this discussion actually argues that the 100 ppm baits are likely to present greater risk to non-target organisms than the 50 ppm baits. In addition, it seems counter-intuitive to argue that bait stations would present greater availability to non-target organisms than broadcast applications without some supporting data.

91 Use of 6-g pellets for ground squirrel control. Ground squirrels are selective feeders much of the year and bait acceptance can greatly limit the time available for applications. Regardless of size, use of pellets instead of grains for spot and broadcast baiting will likely reduce bait acceptability and efficacy from the current formulations. More importantly, concentrating the amounts of active ingredients through use of large pellets may increase the potential primary and secondary risks to non-target mammals, thus offsetting the potential benefit of reduced risks to birds. Risk to non-target mammals

[7] Ibid.

Page RRTF comment

could be increased for several reasons. Use of larger baits will make it easier for non-target mammals, such as coyotes and Kit foxes, to obtain a lethal dose through direct ingestion of pellets.

EFED response: This discussion has been deleted from the document.

93 Use pattern and market share. The Decision Table Analysis ranks the relative hazard of the different active ingredients, but does not estimate exposure, without which risk cannot be estimated. The assumption of equal exposure is totally inappropriate considering the divergent use patterns of products included in this analysis and the high market share held by certain active ingredients. Use pattern is a key factor in any pesticide risk assessment and the exposure is use pattern and often chemical-specific. Brodifacoum (50 ppm), bromadiolone (50 ppm), difethialone (25 ppm), diphacinone (50 ppm), chlorophacinone (50 ppm), bromethalin (100 ppm), cholecalciferol (750 ppm), warfarin (250 ppm), and zinc phosphide (20,000 ppm) baits[1] are all registered for "commensal uses" in the U.S. Commensal use is defined as "in and around buildings, transport vehicles and other manmade structures." Commensal rodents exist because man has provided highly desirable conditions for them to do so (*i.e.*, structures which provide food, water, and/or harborage). In the absence of control measures, commensal rodent populations will escalate because the highly favorable environment provided by man is not balanced by the rodents' natural predators. Farmers, consumers, and professional exterminators for the protection of health and property from commensal rodents use commensal use rodenticides. Commensal rodents typically include the house mouse, the Norway rat, and the roof rat. In some instances, other rodent species, *e.g.*, the deer mouse, can become commensal (*i.e.*, invade structures). Certain rodenticides are also approved for field uses. Field use constitutes use against rodents living "in the field," *i.e.*, not associated with man-made structures. Most typically these rodenticides are used for crop protection, but can also be used against public health pests (*e.g.*, California ground squirrel control for plague prevention). Zinc phosphide bait (typically 20,000 ppm) is the most widely used, being federally registered for a range of uses against a comparatively broad range of rodent and related pests. Some Section 24(c) registrations exist for diphacinone and chlorophacinone and also for some non-federally registered uses of zinc phosphide. Warfarin was recently approved for use against moles below ground. A below ground use diphacinone pocket gopher bait was federally registered, but it is unclear whether this registration is still active. There was also a 24(c) for cholecalciferol that is inactive. A few highly specialized uses also exist for certain products for the purpose of natural ecosystem restoration. Brodifacoum has been used on uninhabited islands in the U.S. and elsewhere to remove non-native rats (arriving originally by ship) that predate and significantly endanger local fauna, typically birds. Diphacinone is used in Hawaii for controlling mongoose and rats that predate native birds. These uses are highly regulated, being carried out by government personnel only, and constitute an extremely small proportion of overall rodenticide use. There are

Page RRTF comment

no other field uses approved in the U.S. for brodifacoum, and no field uses at all for bromadiolone, difethialone, or bromethalin.

EFED response: As previously noted, the risk assessment is based on the available data. Registrants have not submitted the data that would be needed to assess the probability of exposure. These data have been outlined in a section on *Uncertainty and Data Needs*. in the revised assessment.

96 Incorrect term. The term PCO's is used and this term is not defined and is incorrect. *See* discussion above.

EFED response: Previously addressed.

127 & 128 Missing data. Where no data were available, the specific measure of effect was not included in the analysis for that particular active ingredient. This causes an over weighting of data for those measures of effect where data were available.

EFED response: Missing data does add uncertainty to the results of the assessment. This is acknowledged and the data needed to refine this assessment are presented in a section on *Uncertainty and Data Needs*. In addition, many of the studies required in the Rodenticide Cluster Reregistration Eligibility Decision (RED) have not yet been submitted, even though the RED was issued in July, 1998.

134 Correct calculation error. Attachment 1, Results of the Comparative Analysis, Step 3, Substep B, the entry for Bromethalin 100 mg should read ((400.0-2.30)/400)*5=4.97, the LD50 for Bromethalin from Table 1 is 2.30

EFED response: The necessary changes have been made.

135 Correct calculation error. Attachment 1, Results of the Comparative Analysis, Step 4, the entry for Bromethalin 100 mg should read 0.04+4.97=5.01, the sum from Step 3, Substep A, and Substep B.

EFED response: The necessary correction has been made.

135 Correct calculation error. Attachment 1, Results of the Comparative Analysis, Step 4, the entry for Diphacinone 100 mg should read 0.10+2.50=2.60, a simple math computation error, this may or may not have effects on the overall hazard assessment.

EFED response: The sum of the weighted average values for Diphacinone 100 mg should be 0.01+2.50= 2.51. No change was made.

Page RRTF comment

147 HD_5 data. The method used to extrapolate the HD_5 (50%) from one bait concentration to another is not appropriate as it does not take into consideration the slope of the dose-response relationship for the active ingredient. For example, reducing the concentration of active ingredient by 50% will not necessarily reduce toxicity by 50% depending on the slope of the dose-response relationship.

EFED response: The extrapolation from one bait concentration to another does depend upon the slope. However, since slope information was not available, the assumption is that the slope is consistent with a 50% reduction in toxicity when the concentration of the active ingredient is reduced 50%.

151 Correct reference to Table 42. Total incidents of 271 does not match Table 42 summary.

EFED response: The number of incidents has been updated in the revised risk assessment.

153-155 Graphs 9, 10, 11 Lack of correlation. These plots do not show a strong relationship between summary risk values and the number of incidents, suggesting that the two are not highly correlated and that EPA's measures of effect may not be good predictors of incidents. This should not be surprising since EPA's analysis did not account for exposure and product-specific use pattern differences, whereas the incident data better reflect actual exposure, including factors such as market share. Note that the relationships in the graphs will become even weaker once the "corrected" summary values in Table 46 are plotted against the number of incidents. Note also that if data for brodifacoum are removed from the graphs, the data become an almost random scatter gram with no predictive power.

EFED response: This graph was not meant to show an overall correlation between summary risk values and the number of incidents. Rather, the graphs show that the rodenticide baits with the greatest number of reported incidents and the largest summary risk values should appear in the upper left of the graph. In all three graphs brodifacoum is the only bait to appear in this position. Thus, the graph confirms that brodifacoum poses the greatest overall potential risk to birds. The corrected summary values do not significantly weaken this confirmation.